Available online at www.sciencedirect.com
ScienceDirect
Procedia Engineering 110 (2015) 45 – 50
Procedia Engineering
www.elsevier.com/locate/procedia

4th International Conference on Tissue Engineering, ICTE2015

Incidence of temperature and indenter diameter on the mechanical response of skin during indentation test

Jesica Isaza[a], Juan Ramirez[a]*

[a]*Facultad de Minas, Universidad Nacional de Colombia, Medellín 050041, Colombia*

Abstract

Introduction: In vivo tests and design of experiment were carried out to determine the influence of indenter diameter and temperature on the mechanical response of soft tissue.
Material and methods: This study proposes an analysis to obtain the Young's modulus of skin through the use of indentation tests in combination with the Hertz's theory for contact. A design of experiments was developed to determine the incidence of two factors: temperature and indenter diameter, on the mechanical behavior of the skin.
Results: The factors and their interactions are not statistically significant with a p-value higher than 0.05.
Discussion/conclusions: The mean value (±SD) obtained for all eight measurements on the volunteer subject was 28.5 ± 6.9 kPa for E, Young's modulus.

Peer-review under responsibility of IDMEC-IST

Keywords: Young's modulus, human skin, design of experiments, experimental scale.

1. Introduction

Knowledge of the mechanical properties of soft tissues is of great interest for many different medical applications such as medical procedures that use computers and medical images for diagnosis [1]; cancer diagnosis and treatment planning [2], or *in silico* simulations of clinical disorders [3]. The assessment of tissue elasticity has been used for medical practice as an indicator of the onset and progression of diseases in certain organs. An example is the palpation technique used in the exploration of lymph nodes, skin, prostate, breast and abdominal regions. For instance, the

* Corresponding author. Tel.: +57 4 430 9262; fax: +57 4 430 90000.
E-mail address: jframirp@unal.edu.co

Peer-review under responsibility of IDMEC-IST
doi:10.1016/j.proeng.2015.07.008

evolution of diseases as emphysema, tumors [4] atherosclerosis [5], arthritis [6], and others, is associated with the increase in stiffness of the affected tissues [2,5]. However, the lack of quantitative tests does not allow identifying the evolution of the disease according to the specific mechanical properties.

Some *in vivo* tests allow determining the behavior of biological tissues. These experiments are restricted or limited to non-invasive tests and are expensive [7–9]. When *in vivo* tests are not possible, *in vitro* experiments can be made [10], but in these cases simplified variables and less accurate results are obtained since they hardly reproduce the actual conditions of the biological tissues. The indentation test has been used by [11−18] as a tool to determinate the material mechanical properties.

The literature review shows that there are different responses when the experimental scale is changed to perceive the individual mechanical behavior of each skin layer [19–21]. Hendriks et. al. [22,23] varying their aperture size for suction experiments to know the contributions of different skin layers to the mechanical behavior of human skin *in vivo*. They present methods to establish individual properties from different experimental response but in those studies they have not analyzed if there are incidence of the experimental scale on the mechanical properties of the multilayer tissue or skin. Thus, our aim was to establish if two indenter diameters and its temperature affect the mechanical response of the multilayer soft tissues, specifically the skin (a layer of cutis, hypodermis and muscle).

2. Method

The experiment was initially restricted to be performed as an in vivo indentation test on skin, since reliable force and displacement values can be obtained without altering the skin composition, the location and the pre-stress of the skin. The indentation test was conducted using a texturometer, it can be seen in figure 1. This is a device for measuring the normal forces applied by a stainless steel indenter to a sample. During the indentation, the force variation is measured at the same time with the indentation depth.

A design of experiments was carried out to decide which tests or treatments will be performed and how many replicas of each are required to obtain the maximum information at the lowest cost [24]. A factorial experiment was designed to identify if there is any incidence of the experimental parameters over the soft tissues mechanical response. The main parameters considered in this study are: Indenter diameter (A), may modify the experimental scale; and Indenter temperature (B), may contribute to skin stiffness.

A factorial experiment of two factors, with two replicas and two blocks was proposed, leading to a total of eight runs. Each factor is studied in two levels of experimentation, which by convention are called "low" (-1) and "high" (+1). Blocks in experimental designs minimize bias and error variance due to disturbing factors, the block of this experiment was indenter velocity: Block 1, 0.1mm/s and block 2, 3mm/s, it was defined in order to establish differences between results curves and find which is easier to interpret. The experimental conditions for each block were homogenous.

Table 1. Factors and their levels of the design of experiment

Factor	Description	Low (*-1*)	High (*+1*)
A	Indenter diameter	6.35mm	2
B	Indenter temperature	14°C – 17°C	23°C – 26°C6

For the experiment, a balanced ANOVA was run to determine if there was an influence of the diameters, and its interaction with the temperature on the mechanical response. The indenter diameter modifies the experimental scale and should affect the mechanical response.

The experimental forces are useful to calculate an equivalent Young's modulus, and it can be used as an appropriated comparison value. Moreover, the response of the experiment was an equivalent Young's modulus that was analytically found using Hertz's theory for contact between a sphere of radius a and an elastic half-space. The applied force *P* is related to the displacement *h* by

$$P = \frac{4}{3} E^* a^{1/2} h^{3/2} \tag{1}$$

Where

$$\frac{1}{E^*} = \frac{(1-v^2)}{E} + \frac{(1-v'^2)}{E'} \tag{2}$$

And E, E' are the elastic moduli and v, v' the Poisson's ratios associated with each body.

The indentation tests were carried out on the right ventral forearm zone of right-handed person (Fig. 1). This location is easily accessible, relatively flat, and less disturbed by the natural movements of the body. A spherical tip indenter was selected, since rounding edges minimizes stress concentrations and eliminates any possibility of pain. In this region, the epidermis is thin (less than 80 µm [25]), and the thickness of the hypodermis (about 0.8 mm) is smaller than the thickness of the dermis (known to be between 1.2 mm and 1.5 mm [25]). Therefore, an indentation depth of 5mm. exceeds twice the thickness of the first two layers to guarantee that there is skin tissue response.

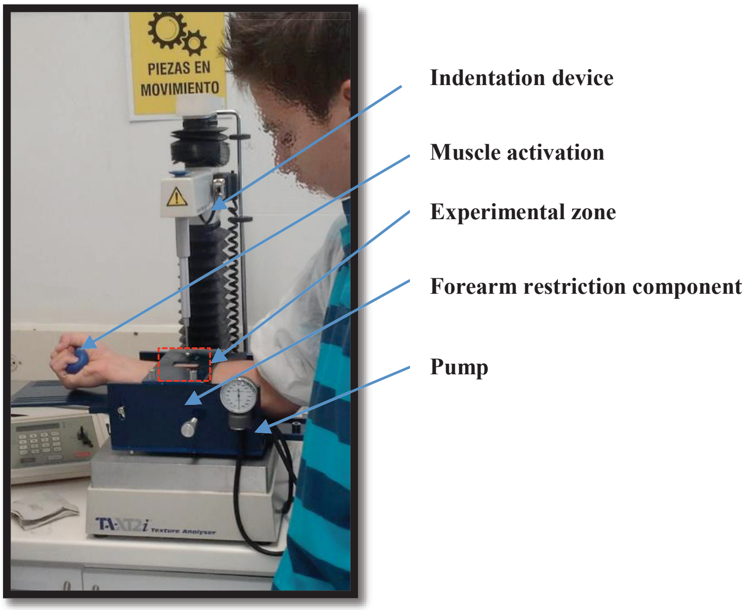

Fig. 1. Experimental assembly: Device for ensuring the forearm, mechanism to activate the muscle, and experimentation exposed area are indicated

3. Results

Although the skin is not linear elastic, this is a preliminary approximation to estimate the incidence of the indenter size on the mechanical response of skin. Hence, it was determined the Young's modulus for the multilayer assembly cutis-hypodermis-muscle for each run.

According to equation (1), E^* values were obtained as the slope of the line resulting from the linear regression between the P against $(4/3)\, a^{1/2}\, h^{3/2}$. In Fig. 2 can be seen curves for each treatment and one example of the trend line for T5 (Treatment 5) when the slope value E^* is 0.0516MPa. Table 2 shows the design of experiment and the respective Young's modulus E, obtained from equation (2).

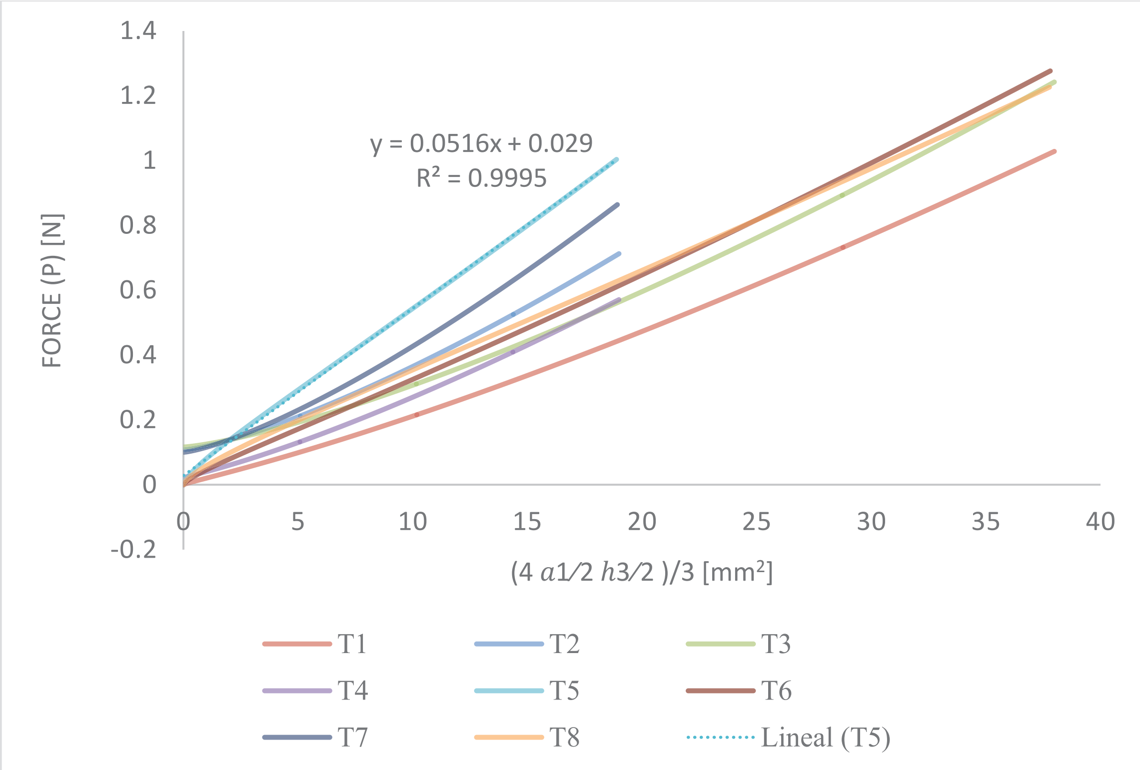

Fig. 2. Representative graphic of skin E*

The Young's moduli values are presented in the following table:

Table 2. Results of the experiment

DOE treatment	Indenter diameter (*mm*)	Indenter temperature (*°C*)	Indentation velocity (*mm/s*)	Young's modulus (*kPa*)
T1	25.4	15	0.1	22,34
T2	6.35	15	0.1	26,46
T3	25.4	25	0.1	24,61
T4	6.35	25	0.1	23,86
T5	6.35	25	3.0	43,34
T6	25.4	15	3.0	27,72
T7	6.35	15	3.0	33,60
T8	25.4	25	3.0	26,46

The balanced ANOVA, from the data shown in table 3, indicated with a test significance level of 5% that factors evaluated on the Young's modulus are not statistically significant because the p-value is higher than 0.05. Moreover, the modulus average value was of 28.5 ± 6.9 kPa and the experiment presented a good reliability with an R^2 of 73.23%.

Table 3. ANOVA

Sources	Degree of Freedom	Sum of Squares	Mean Squares	Fo	P - Value
Blocks	1	0.00014325	0.00014325	4.87	0.115
Principal effects	2	0.00009361	0.00004680	1.59	0.338
Temperature.	1	0.00000830	0.00000830	0.28	0.632
Diameter	1	0.00008531	0.00008531	2.90	0.187

2-Interactions of factors	1	0.00000470	0.00000470	0.16	0.716
Temperature*Indenter	1	0.00000470	0.00000470	0.16	0.716
Residual error	3	0.00008829	0.00002943		
Total	7	0.00032985			

The assumptions of normal distribution, equal variances, and randomization of the residuals were checked to guarantee the validity of the design of experiments conclusions.

The statistical model for factorial experiment with two factors (A and B) and n replicates is:

$$y_{ijk} = \mu + \tau_i + \beta_j + (\tau\beta)_{ij} + \delta_k + \varepsilon_{ijk} \begin{cases} i = 1,2,...,a \\ j = 1,2,...,b \\ k = 1,2,...,n \end{cases} \quad (3)$$

Where τ_i, β_i, and $(\tau\beta)_{ij}$ represent the effect of factors A, B and the AB interaction, respectively. And δ_k is the effect of the kth block, ε_{ijk} is a random error component and μ is the overall mean effect [24]. It is not necessary to refer a regression model due to there is no statistical significant factors.

4. Discussion

Skin can be modeled like a not linear elastic tissue. However, this study has a good reliability and is useful as a preliminary approximation to estimate the incidence of the indenter size on the mechanical response and to establish a Young's modulus of skin.

It is not possible to talk about a unique value reported in the literature for skin mechanical properties. In this study, the value found is 28.5kPa, this value has the same order of magnitude of the ones reported by other authors for volar forearm. Xing Liang and Stephen A. Boppart [26] found a Young's modulus from the volar forearm of 101.180 kPa from dynamic optical coherence elastography. G. Boyer et al. [27] found a reduced Young's modulus with an air flow force of 10 mN, in a device called Tonoderm, of 14.38 ± 3.61 kPa for the youngest group and 6.20 ± 1.45 kPa for the oldest group of women. The average value of the skin Young's modulus, found by Pailler-Mattei et al [11], between 4.5 kPa and 8 kPa for indentation tests.

Different skin layers have contribution on the mechanical behavior of human skin in vivo [22,23], layer thickness is statistically significant on the mechanical response of the multilayer tissues and, clearly, the precision of the elastic modulus also depends on this factor [28]. Future works can include the analysis of indenter size in combination with real thickness of skin layers, on a definitive manner, the effect of this factor on the skin response.

The effect of different experimental conditions to determine mechanical properties of soft tissue had not been simultaneously analyzed. However, future studies must establish the incidence of several experimental conditions acting at the same time, like: room and indenter temperature, gender, muscle activation, velocity, etc. that can affect the constitutive equations that represent the mechanical response of the skin (cutis, hypodermis and muscle).

Ethical approval

All procedures were performed according to a protocol approved by Committee for Research Ethics on Living Creatures at National University of Colombia (Act number: 2-2013 April).

Acknowledgements

We thank the participants for their availability.

References

[1] J.-M. Schwartz, M. Denninger, D. Rancourt, C. Moisan, D. Laurendeau, Modelling liver tissue properties using a non-linear visco-elastic model for surgery simulation, Med. Image Anal. 9 (2005) 103–112. doi:10.1016/j.media.2004.11.002.

[2] F.. Carter, T.. Frank, P.. Davies, D. McLean, A. Cuschieri, Measurements and modelling of the compliance of human and porcine organs, Med. Image Anal. 5 (2001) 231–236. doi:10.1016/S1361-8415(01)00048-2.

[3] P.A. Forbes, D.S. Cronin, Y.C. Deng, Multi-scale human body model to predict side impact thoracic trauma, Int. J. Crashworthiness. 11 (2006) 203–216. doi:10.1533/ijcr.2005.0391.

[4] M. Kaneko, C. Toya, M. Okajima, Active Strobe Imager for Visualizing Dynamic Behavior of Tumors, in: 2007 IEEE Int. Conf. Robot. Autom., 2007: pp. 3009–3014. doi:10.1109/ROBOT.2007.363929.

[5] G.A. Holzapfel, G. Sommer, P. Regitnig, Anisotropic Mechanical Properties of Tissue Components in Human Atherosclerotic Plaques, J. Biomech. Eng. 126 (2004) 657–665. doi:10.1115/1.1800557.

[6] K. Rome, Mechanical properties of the heel pad: current theory and review of the literature, The Foot. 8 (1998) 179–185. doi:10.1016/S0958-2592(98)90026-8.

[7] Martin Kauer, Inverse finite element characterization of soft tissues with aspiration experiments, SWISS FEDERAL INSTITUTE OF TECHNOLOGY, 2001. http://e-collection.library.ethz.ch/view/eth:24157 (accessed October 27, 2011).

[8] D.B. Plewes, J. Bishop, A. Samani, J. Sciarretta, Visualization and quantification of breast cancer biomechanical properties with magnetic resonance elastography, Phys. Med. Biol. 45 (2000) 1591–1610.

[9] S. Portnoy, I. Siev-Ner, N. Shabshin, A. Kristal, Z. Yizhar, A. Gefen, Patient-specific analyses of deep tissue loads post transtibial amputation in residual limbs of multiple prosthetic users, J. Biomech. 42 (2009) 2686–2693. doi:10.1016/j.jbiomech.2009.08.019.

[10] M. Van Loocke, C.G. Lyons, C.K. Simms, Viscoelastic properties of passive skeletal muscle in compression: Stress-relaxation behaviour and constitutive modelling, J. Biomech. 41 (2008) 1555–1566. doi:10.1016/j.jbiomech.2008.02.007.

[11] C. Pailler-Mattei, S. Bec, H. Zahouani, In vivo measurements of the elastic mechanical properties of human skin by indentation tests, Med. Eng. Phys. 30 (2008) 599–606. doi:10.1016/j.medengphy.2007.06.011.

[12] J. Su, H. Zou, T. Guo, The Study of Mechanical Properties on Soft Tissue of Human Forearm In Vivo, in: IEEE, 2009: pp. 1–4. doi:10.1109/ICBBE.2009.5163671.

[13] A. Samani, D. Plewes, A method to measure the hyperelastic parameters of ex vivo breast tissue samples, Phys. Med. Biol. 49 (2004) 4395–4405.

[14] T. Kaster, I. Sack, A. Samani, Measurement of the hyperelastic properties of ex vivo brain tissue slices, J. Biomech. 44 (2011) 1158–1163. doi:10.1016/j.jbiomech.2011.01.019.

[15] J.J. O'Hagan, A. Samani, Measurement of the hyperelastic properties of tissue slices with tumour inclusion, Phys. Med. Biol. 53 (2008) 7087–7106. doi:10.1088/0031-9155/53/24/006.

[16] S.P. DiMaio, S.E. Salcudean, Needle insertion modeling and simulation, IEEE Trans. Robot. Autom. 19 (2003) 864–875. doi:10.1109/TRA.2003.817044.

[17] J. Kim, M.A. Srinivasan, Characterization of Viscoelastic Soft Tissue Properties from In Vivo Animal Experiments and Inverse FE Parameter Estimation, in: J.S. Duncan, G. Gerig (Eds.), Med. Image Comput. Comput.-Assist. Interv. – MICCAI 2005, Springer Berlin Heidelberg, 2005: pp. 599–606. http://link.springer.com/chapter/10.1007/11566489_74 (accessed June 14, 2013).

[18] D.L. Bader, P. Bowker, Mechanical characteristics of skin and underlying tissues in vivo, Biomaterials. 4 (1983) 305–308. doi:10.1016/0142-9612(83)90033-9.

[19] M.A.F. Kendall, Y.-F. Chong, A. Cock, The mechanical properties of the skin epidermis in relation to targeted gene and drug delivery, Biomaterials. 28 (2007) 4968–4977. doi:10.1016/j.biomaterials.2007.08.006.

[20] F.M. Hendriks, D. Brokken, C.W.J. Oomens, Mechanical Properties of Different Layers of Human Skin, Mate. (n.d.). http://xa.yimg.com/kq/groups/20011190/1545366489/name/Proprietati+mecanice+de+tradus.pdf (accessed June 13, 2013).

[21] M.L. Crichton, B.C. Donose, X. Chen, A.P. Raphael, H. Huang, M.A.F. Kendall, The viscoelastic, hyperelastic and scale dependent behaviour of freshly excised individual skin layers, Biomaterials. 32 (2011) 4670–4681. doi:10.1016/j.biomaterials.2011.03.012.

[22] F.M. Hendriks, D. Brokken, C.W.J. Oomens, F.P.T. Baaijens, Influence of hydration and experimental length scale on the mechanical response of human skin in vivo, using optical coherence tomography, Skin Res. Technol. 10 (2004) 231–241. doi:10.1111/j.1600-0846.2004.00077.x.

[23] F.M. Hendriks, D. Brokken, C.W.J. Oomens, D.L. Bader, F.P.T. Baaijens, The relative contributions of different skin layers to the mechanical behavior of human skin in vivo using suction experiments, Med. Eng. Phys. 28 (2006) 259–266. doi:10.1016/j.medengphy.2005.07.001.

[24] D.C. Montgomery, Design and Analysis of Experiments, John Wiley & Sons, 2008.

[25] F.M. Hendriks, D. Brokken, J.T.W.M. Van Eemeren, C.W.J. Oomens, F.P.T. Baaijens, J.B. a. M. Horsten, A numerical-experimental method to characterize the non-linear mechanical behaviour of human skin, Skin Res. Technol. 9 (2003) 274–283. doi:10.1034/j.1600-0846.2003.00019.x.

[26] X. Liang, S.A. Boppart, Biomechanical Properties of In Vivo Human Skin From Dynamic Optical Coherence Elastography, IEEE Trans. Biomed. Eng. 57 (2010) 953–959. doi:10.1109/TBME.2009.2033464.

[27] G. Boyer, C. Pailler Mattei, J. Molimard, M. Pericoi, S. Laquieze, H. Zahouani, Non contact method for in vivo assessment of skin mechanical properties for assessing effect of ageing, Med. Eng. Phys. 34 (2012) 172–178. doi:10.1016/j.medengphy.2011.07.007.

[28] J. Isaza, J. Ramírez, P. Fuentes, Incidencia del espesor y rigidez de dos materiales en configuración multicapa sobre la caracterización mecánica mediante análisis inverso del métodos de lso elementos finitos combinado con ensayo de indentación, in: La Plata, Argentina, 2013.